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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/780,349	02/17/2004	Galla Chandra Rao	IMMC 307 PCT/US	9963

40541 7590 12/20/2005

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EXAMINER	
BARNHART, LORA ELIZABETH	
ART UNIT	**PAPER NUMBER**
1651	

DATE MAILED: 12/20/2005

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	10/780,349	RAO ET AL.	
	Examiner	Art Unit	
	Lora E. Barnhart	1651	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *09 November 2005*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-145* is/are pending in the application.

4a) Of the above claim(s) *5,8,9,20,23,24,31-138 and 141-145* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1-4,6,7,10-20,22,23,25,139 and 140* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☒ The specification is objected to by the Examiner.

10)☒ The drawing(s) filed on *17 February 2004* is/are: a)☐ accepted or b)☒ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: _____.

DETAILED ACTION

Election/Restrictions

Applicant's election without traverse of Group I, claims 1-30, 139, and 140, in the reply filed on 11/9/05 is acknowledged. Applicant's election without traverse of the species EDTA, imidazolidinyl urea, and chromium in the same reply is acknowledged.

Claims 31-138 and 141-145 are withdrawn from further consideration pursuant to 37 CFR 1.142(b) as being drawn to a nonelected invention, there being no allowable generic or linking claim. Claims 5, 8, 9, 20, 23, and 24 are withdrawn from further consideration pursuant to 37 CFR 1.142(b) as being drawn to a nonelected species, there being no allowable generic or linking claim. Examination will commence on claims 1-4, 6, 7, 10-19, 21, 22, 25-30, 139, and 140 ONLY, to the extent that they read on the elected species.

Specification

The use of the trademarks "CYTO-CHEX", "STABILCYTE", and "TRANSFIX" has been noted in this application. These trademarks (and all trademarks) must be accompanied by the generic terminology such that they are particularly defined. Although the use of trademarks is permissible in patent applications, the proprietary nature of the marks should be respected and every effort made to prevent their use in any manner which might adversely affect their validity as trademarks.

Drawings

The drawings are objected to because Figures 3-5 appear to comprise photographs that are grainy and indecipherable. Corrected drawing sheets in

compliance with 37 CFR 1.121(d) are required in reply to the Office action to avoid abandonment of the application. Any amended replacement drawing sheet should include all of the figures appearing on the immediate prior version of the sheet, even if only one figure is being amended. The figure or figure number of an amended drawing should not be labeled as "amended." If a drawing figure is to be canceled, the appropriate figure must be removed from the replacement sheet, and where necessary, the remaining figures must be renumbered and appropriate changes made to the brief description of the several views of the drawings for consistency. Additional replacement sheets may be necessary to show the renumbering of the remaining figures. Each drawing sheet submitted after the filing date of an application must be labeled in the top margin as either "Replacement Sheet" or "New Sheet" pursuant to 37 CFR 1.121(d). If the changes are not accepted by the examiner, the applicant will be notified and informed of any required corrective action in the next Office action. The objection to the drawings will not be held in abeyance.

Claim Rejections - 35 USC § 112

The following is a quotation of the second paragraph of 35 U.S.C. 112:

> **The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.**

Claims 1-4, 6, 7, 10-19, 22, 23, 25-20, 139, and 140 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

Claim 1 recites a composition for preserving biological specimens consisting of an anticoagulating agent and a stabilizing agent. It is not clear, however, whether the

composition or the specimens consist of an anticoagulating agent and a stabilizing agent. Similarly, claim 16 recites a composition for preserving blood samples suspected to contain circulating tumor cells consisting of an anticoagulating agent and a stabilizing agent. It is not clear, however, whether the composition, the blood sample, or the cells are meant to consist of an anticoagulating agent and a stabilizing agent. Clarification is required. Because claims 2-4, 6, 7, 10-15, 17-19, 22, 23, 25-20, 139, and 140 depend variously from indefinite claims 1 and 16 and do not clarify the point of confusion, they must also be rejected under 35 U.S.C. 112, second paragraph. In the interest of compact prosecution, claims 1 and 16 have been interpreted by the examiner as being drawn to compositions consisting of an anticoagulating agent and a stabilizing agent, as these terms are defined at pages 7 and 8 of the specification.

Claims 4 and 19 are confusing in that they require that the anticoagulating agent be a complexing agent; the term "complexing agent" is not defined in the specification. It is therefore not clear how claim 4 further limits claim 1 or how claim 19 further limits claim 15. Clarification is required.

Claims 6 and 21 are confusing in that they require that the stabilizing agent be a "formaldehyde donor", but this term is not described in the specification. Clarification is required.

Claims 7 and 22 are confusing in that they require that the formaldehyde donor be imidazolidinyl urea, but imidazolidinyl urea does not appear to comprise any moiety resembling formaldehyde. It is not clear how this compound could be a formaldehyde donor. Clarification is required.

Claims 10 and 25 are confusing in that they require that the stabilizing agent be a formaldehyde donor **combined with** a heavy metal element, but the nature of the combination is not defined in the specification or the claims. This limitation is particularly confusing in light of the fact that claims 1 and 16 require that the composition consist only of an anticoagulating agent and a stabilizing agent. Clarification is required.

Claims 12-15, 27-30, 139, and 140 are confusing in that they depend from claim 1, which is drawn to a composition **consisting of** two components, but require that the composition also include a third component, *i.e.* an "additional stabilizing agent." The transitional phrase "consisting of" excludes any element, step, or ingredient not specified in the claim. *In re Gray*, 53 F.2d 520, 11 USPQ 255 (CCPA 1931); *Ex parte Davis*, 80 USPQ 448, 450 (Bd. App. 1948); see M.P.E.P. § 2111.03. Clarification is required. In the interest of compact prosecution, these claims have been interpreted as being drawn to embodiments wherein the parent compositions (those of claims 1 and 16) consist of a stabilizing agent, an anticoagulant, and an additional stabilizing agent.

Claims 13-15 and 28-30 are further confusing in that they require that the molecular weight of polyethylene glycol to be, for example, "in the range of about 1000 to about 35000", but no units are provided for these measurements. Clarification is required.

Claims 139 and 140 recite the limitation "the specimen volume" in line 3 of each claim. There is insufficient antecedent basis for this limitation in the claim. Neither claim 1 nor claim 16 recite a specimen volume. Clarification is required.

Claims 139 and 140 recite "preferred" and "more preferred" conditions, which do not precisely define the metes and bounds of the claims. It is not clear whether any conditions other than the recited conditions are part of the claimed invention. Clarification is required.

Claim Rejections - 35 USC § 102

The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless –
>
> (b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

Claims 1-4, 6, 7, 12-19, 22, 23, 27-20, 139, and 140 are rejected under 35 U.S.C. 102(b) as being anticipated by Ryan (1995, U.S. Patent 5,459,073; reference A) taken in light of information from Sigma-Aldrich (reference U). The claims are drawn to compositions comprising an anticoagulating agent and a stabilizing agent. In some dependent claims, the anticoagulating agent is a chelating agent, for example ethylenediamine tetraacetic acid (EDTA), or a complexing agent. In some dependent claims, the stabilizing agent is a formaldehyde donor, for example imidazolidinyl urea (IDU).

Ryan teaches a composition comprising 3% IDU, 0.3% PEG (molecular weight 20,000 Daltons), and PMSF (phenylmethylsulfonyl fluoride, a protease inhibitor) in phosphate-buffered saline (PBS) that itself comprises EDTA (Example XII; column 11, lines 8-10). This composition has been interpreted as **consisting of** an anticoagulating agent and a stabilizing agent in accordance with the definitions of these two terms in the

specification (page 7, line 6, through page 8, line 7). An "anticoagulating agent" is defined as a **composition** that is added to a biological specimen for the purpose of inhibiting undesired coagulation. A "stabilizing agent" is defined as a **composition** capable of preserving target cells of interest present in a biological specimen. Since the definitions of "anticoagulating agent" and "stabilizing agent" recite compositions, then in accordance with the specification, the claimed composition may consist of two or more compositions, as long as the constituent compositions fulfill the requirements of the definitions provided in the specification. In this case, the anticoagulant is EDTA-PBS, and the stabilizing agent is a composition comprising IDU (a fixative), PEG (which reduces damage to cells during processing; column 10, lines 27-29), and PMSF (which prevents the degradation of cells by proteases released therefrom; see reference U).

M.P.E.P. § 2111.02 reads, "If the body of a claim fully and intrinsically sets forth all of the limitations of the claimed invention, and the preamble merely states, for example, the purpose or intended use of the invention, rather than any distinct definition of any of the claimed invention's limitations, then the preamble is not considered a limitation and is of no significance to claim construction." As such, the limitations "for preserving biological specimens" and "for preserving blood samples suspected to contain circulating tumor cells" have been given little patentable weight.

The prior art made of record and not relied upon is considered pertinent to applicant's disclosure. U.S. Patent 5,849,517 (1998, reference B) to Ryan teaches additional experiments and applications in which the composition of the Ryan '073 patent is administered to cells. U.S. Patents 4,140,759 (1979, reference C) to Mausner

and 4,658,839 (1987, reference D) to Dallal et al. teach compositions comprising IDU, EDTA, and PEG (claim 16 and column 7, lines 4-45, respectively).

Claim Rejections - 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

The factual inquiries set forth in *Graham* **v.** *John Deere Co.*, 383 U.S. 1, 148 USPQ 459 (1966), that are applied for establishing a background for determining obviousness under 35 U.S.C. 103(a) are summarized as follows:

1. Determining the scope and contents of the prior art.
2. Ascertaining the differences between the prior art and the claims at issue.
3. Resolving the level of ordinary skill in the pertinent art.
4. Considering objective evidence present in the application indicating obviousness or nonobviousness.

This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. 103(a), the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligation under 37 CFR 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later invention was made in order for the examiner to consider the applicability of 35 U.S.C. 103(c) and potential 35 U.S.C. 102(e), (f) or (g) prior art under 35 U.S.C. 103(a).

Claims 1-4, 6, 7, 10-19, 22, 23, 25-20, 139, and 140 are rejected under 35 U.S.C. 103(a) as being unpatentable over Ryan (reference A). The claims are drawn to compositions comprising an anticoagulating agent and a stabilizing agent. In some dependent claims, the anticoagulating agent is a chelating agent, for example ethylenediamine tetraacetic acid (EDTA), or a complexing agent. In some dependent claims, the stabilizing agent is a formaldehyde donor, for example imidazolidinyl urea (IDU), which may be combined with a heavy metal element, for example chromium. In some dependent claims, the composition comprises an additional stabilizing agent, polyethylene glycol (PEG), of a particular molecular weight and in a particular concentration.

Ryan teaches various compositions for fixing and stabilizing cells and tissues (Abstract). One such composition comprises 1% IDU in phosphate-buffered saline that comprises EDTA (Example XII; column 10, lines 46-48). Ryan further teaches adding cells to said composition, rinsing and repeating numerous times, and eventually placing the cells into a composition comprising EDTA, 3% IDU, and 0.3% PEG of molecular weight 20,000 Daltons (column 11, lines 5-7). Ryan also teaches a composition comprising 2-bromo-2-nitropropane-1,3-diol (Bronopol), IDU, zinc sulfate heptahydrate, and sodium citrate dihydrate (Example X; lines 18-21). Ryan suggests that the compositions of the invention further comprise mordants (reagents that fix dyes to cells), which may include zinc or chromium salts, *inter alia* (column 6, lines 48-57). Ryan does not teach a single composition consisting of an anti-coagulating agent (for example,

EDTA), a stabilizing agent (for example, IDU), an additional stabilizing agent (for example, PEG), and a heavy metal element (for example, chromium).

The Example X composition of Ryan comprises two stabilizing agents (Bronopol and IDU) and a heavy metal element (zinc). The Example XII composition of Ryan comprises two stabilizing agents (IDU and PEG) and an anticoagulating agent (EDTA). A person of ordinary skill in the art would have had a reasonable expectation of success in adding the heavy metal element of the Example X composition to the Example XII composition because Ryan suggests that any of the compositions may further comprise a mordant, such as a heavy metal (column 6, lines 48-57). The skilled artisan would have been motivated to add a heavy metal element for the expected benefit that histological dyes (such as those at column 9, lines 40-50) are better fixed to the cells being preserved.

The selection of heavy metal element would have been a routine matter of optimization on the part of the artisan of ordinary skill, said artisan recognizing that Ryan teaches that zinc, chromium, and other heavy metal elements are functional equivalents (column 6, lines 54-57). A holding of obviousness over the cited claims is therefore clearly required.

It would therefore have been obvious to a person of ordinary skill in the art at the time the invention was made to add chromium to the Example XII composition of Ryan (which comprises EDTA, IDU, and 0.3% PEG-20,000) because Ryan suggests adding a mordant (for example, chromium) to any of the fixatives taught (column 6, lines 48-57).

Therefore, the invention as a whole would have been prima facie obvious to a person of ordinary skill at the time the invention was made.

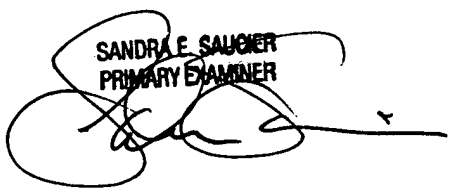
No claims are allowed. No claims are free of the art.

Applicant should specifically point out the support for any amendments made to the disclosure, including the claims (MPEP 714.02 and 2163.06). Due to the procedure outlined in MPEP § 2163.06 for interpreting claims, it is noted that other art may be applicable under 35 U.S.C. § 102 or 35 U.S.C. § 103(a) once the aforementioned issue(s) is/are addressed.

Applicant is requested to provide a list of all copending applications that set forth similar subject matter to the present claims. A copy of such copending claims is requested in response to this Office action.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Lora E. Barnhart whose telephone number is 571-272-1928. The examiner can normally be reached on Monday-Friday, 8:00am - 4:30pm.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Michael G. Wityshyn can be reached on 571-272-0926. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.



Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

Lora E Barnhart

SANDRA E. SAUCIER
PRIMARY EXAMINER